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CHEMICAL CONSTITUENTS OF *Cordyceps neovolkiana* DL0004

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The genus *Cordyceps* is widely distributed in South Asia, Europe, and North America. *In vitro* and *in vivo* studies of this genus have validated its medicinal properties [1]. The phytochemical investigation of this genus have resulted in over 200 bioactive metabolites having various scaffolds such as saccharides, polysaccharides, cylopeptides, sterols, polyketide, terpenoids, and alkaloids [1, 2]. The two most studied members of this genus, *C. sinensis* and *C. militaris,* are valuable traditional Chinese medicines and have been used in the treatment of liver and renal dysfunction and heart and lung diseases [3–7]. Recently, other *Cordyceps* species have gained much chemical and biological attention [3, 8–12]. *Cordyceps neovolkiana* is widely distributed in the South of Vietnam. Phytochemical data of this species are scarce. In this paper, the isolation of 12 compounds from cultures of the titled fungus is described. The chemical structures of the compounds were determined using NMR and MS spectroscopy as well as comparison with data described in the literature. Isolates were elucidated as ergosta-4,6,8(14),22-tetraen-3-one (**1**), ergosterol peroxide (**2**), cerevisterol (**3**), melithasterol B (**4**), brassicasterol (**5**), ergosterol (**6**), ergosterol 3-*O*-β-D-glucopyranoside (**7**), 1-dehydroxycordypyridone (**8**), thymine (**9**), nicotinamide (**10**), uridine (**11**), and 5-methylhaematommic acid (**12**). To the best of our knowledge, all the isolated compounds (**1–12**) were isolated from this species for the first time. The cytotoxicity of the isolates against K562 cell line was evaluated. Compound **1** showed potent activity with IC_{50} 5.24 ± 0.38 μg/mL (doxorubicin, positive control 4.87 ± 0.47 μg/mL). Compounds **2**, **4**, and **6** showed moderate activity with IC_{50} 45.05 ± 1.26, 46.01 ± 3.54, and 34.03 ± 0.32 μg/mL, respectively, while the others showed no activity.

Fungal Material. *Cordyceps neovolkiana* was collected in the Langbiang Mountain, Lam Dong Province. This strain of *C. neovolkiana* was identified by Dr. Minh-Hiep Dinh and stored at the University of Science, Ho Chi Minh City (No. US.F021).

Fermentation and Extraction. After fermentation in liquid medium (consisting of 20% potato extract, 0.05% sucrose, 0.006% peptone, 0.004% yeast extract, 0.0005% K_2HPO_4, and 0.0002 $MgSO_4 \cdot 7H_2O$) with a ratio of 4% seed at 23°C for 40 days, the mycelial biomass was harvested and dried at 50°C. Mycelia of *C. neovolkiana* (1.9 kg) were macerated with ethanol 96% (20 L × 2) at room temperature to provide the crude extract (490 g). Then to the crude extract was added water and the whole successively partitioned into petroleum ether, EtOAc, and *n*-butanol to obtain the PE (7.2 g), EA (85 g), and Bu (52 g) extracts, respectively.

Extraction and Isolation. The extract PE (7.2 g) were fractionated by normal phase CC using a gradient solvent system of *n*-hexane–EtOAc–acetone (10:1:1–4:1:1) as eluent to obtain eight fractions PE1-8. Fraction PE3 (710.0 mg) was rechromatographed by CC using the mobile phase of *n*-hexane–EtOAc-acetone (10:1:1) to provide four compounds **1** (3.9 mg), **2** (41 mg), **5** (3.2 mg), and **6** (140 mg). Fraction PE7 (210.0 mg) was applied to a Sephadex column and eluted with methanol to afford three fractions PE7.1-3. Purification of fraction PE7.3 (87 mg) by C18 reverse phase CC with the solvent system of methanol–water (10:1) gave three compounds, **3** (11 mg), **4** (3.5 mg), and **12** (9 mg).

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